

II. REMARKS

Claims 2, 5-7, 17-19, and 21-41 are pending in the above-identified application. Claims 24 to 41 were withdrawn from examination as a result of a requirement for restriction. Claims 2, 5-7, 17-19 and 21 to 23 were examined and finally rejected.

No claims have been amended. Applicants respectfully request reconsideration and withdrawal of the outstanding rejections.

35 U.S.C. § 103

Claims 2, 5-7, 17-19 and 21-23 remain rejected under 35 U.S.C. § 103 (a) as allegedly unpatentable over either Li et al. or Rothwarf et al. (Reference C27 of Applicant's PTO-1449) in view of Trancard et al. and Epinat et al.

Briefly, and without repeating the stated grounds for rejection as allegedly obvious over the cited art, the Office argued that the cited art would have led a skilled artisan to reasonably expect that since yeast do not endogenously produce the IKK proteins and contain no homologs of the NF- κ B signaling system, a homogenous IKK complex formed from only the heterologously introduced IKK genes would have been expected.

The Office argued that Traincard et al. teach that within eukaryotic systems, no homologs of any of member of the NF-kappaB signaling system (clearly disclosed as including Rel/NF-kappaB subunit genes and IKK gene) has been found within the genomes of *C. elegans* or *Saccharomyces cerevisia*, both of which were fully sequenced genomes at the time of the publication of Traincard et al. Epinat et al. teach that yeast is a convenient host for the reconstitution of the NF-kappaB system since it does not contain an endogenous NF-kappaB activity and that the reconstituted system provide an easy assay for testing stimuli or specific proteins that are postulated to be involved in NF-kappa signaling. Epinat et al. also showed that an expressed I κ B protein could not be phosphorylated in yeast even under similar stimuli to those known to induce I κ B phosphorylation in mammals.

Applicants respectfully traverse. The criteria for evaluating an invention under 35 U.S.C. § 103 is recited in *Graham v. John Deere Co.*, 383 U.S. 1, 148 U.S.P.Q. 459 (1966). In this reported decision, the Supreme Court set forth various factual inquiries and so-called "secondary considerations" or indicia of non-obviousness. The Supreme Court stated:

“Under 103, the scope and content of the prior art are to be determined; differences between the prior art and the claims at issue are to be ascertained; and the level of ordinary skill in the pertinent art resolved. Against this background, the obviousness or nonobviousness of the subject matter is determined. Such secondary considerations as commercial success, long felt but unsolved needs, failure of others, etc., might be utilized to give light to the circumstances (383 U.S. 1, 18) surrounding the origin of the subject matter sought to be patented. As indicia of obviousness or nonobviousness, these inquiries may have relevancy.”

Using these criteria as a guide, Applicants submit that the claimed invention is patentable over the cited art because the combined art does not teach the recited elements and one of skill in the art would not have expected that the claimed system would or could produce the claimed invention even if the prior art was modified as suggested by the Office.

Applicants agree that the cited prior art (namely Traincard et al. and Epenat et al.) teach that no member of the NF-kappaB pathway exists in *Saccharomyces cerevisia* at the time of the application and yeast lacked the ability to phosphorylate the IκB protein. However, in comparing the teachings of the references in combination, Applicants note that they do not teach or suggest that the production of **substantially homogenous and biologically functional IKK protein complex** as recited in the claims. One of skill in the art would not have expected to be able to produce the functional complex because it was known at the time of the effective filing date that yeast does not produce a homolog to the mammalian activating complex. Stated another way, it was known that mammalian systems require phosphorylation for activation (i.e., biological functional complex) by protein kinases and that yeast does not have a homologous system, i.e., yeast does not have analogous “activating” proteins such as TRAF2, RIP, and A20. In support of their position, Applicants direct the Office to Devin et al. (Exhibit A), Zang et al. (Reference C45 of Applicant’s PTO-1449) and Lin et al. (Exhibit B).

Devin et al. teach that the RIP kinase and the TRAF2 protein are essential effectors in the TNF signaling pathway. In response to TNF treatment, the transcription factor NF- κ B is activated and is mediated through activated IKK. Moreover, they teach that IKK activation requires the presence of RIP in the same complex (see Summary and Introduction). This concept is further supported by the prior art publication of Zang et al., which teaches the signaling activation of the IKK signalsome are regulated through binding of NEMO (IKK γ) to RIP and A20 through the p55 TNF receptor complex (see Summary and Introduction). This is further supported by Lin et al., which teaches that the death domain kinase RIP, a key factor in TNF signaling, also plays a pivotal role in TRAIL-induced IKK and JNK activation. Thus, at the time of the effective filing date, one of skill in the art would not have expected that yeast would be capable of producing substantially homogenous and biologically functional IKK complex because yeast lacks all of these necessary activating proteins to produce such activated IKK complex.

Accordingly, because the prior art as a whole taught against the claimed invention and thus, an expectation of success was lacking, Applicants submit that the rejection is in error and respectfully request its withdrawal.

Supplemental Information Disclosure Statement

Attached to this Response is a Supplemental Information Disclosure Statement for consideration and entry into the file.

III. CONCLUSION

Applicants believe that the present application is now in condition for allowance. Favorable reconsideration of the application is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to

Deposit Account No. 50-0872. Should no proper payment be enclosed herewith, as by a check or credit card payment form being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 50-0872. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 50-0872.

Respectfully submitted,

Date

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By

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